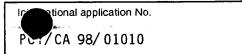


(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference DH/12725.6	FOR FURTHER ACTION	see Notification of T (Form PCT/ISA/220	ransmittal of International Search Report ) as well as, where applicable, item 5 below.
International application No.	International filing date (day	y/month/year)	(Earliest) Priority Date (day/month/year)
PCT/CA 98/01010	29/10/19	98	31/10/1997
Applicant			
CENTRE DE RECHERCHE DU CE	NTRE HOSPITALIER	et al	
This International Search Report has bee according to Article 18. A copy is being tra	n prepared by this Internation ansmitted to the International	al Searching Author Bureau.	rity and is transmitted to the applicant
This International Search Report consists  It is also accompanied by a cop		sheets. cited in this report.	
1. χ Certain claims were found un	searchable(see Box I).		
2. Unity of invention is lacking(s	see Box II).		
The international application co- international search was carried			acid sequence listing and the
filed	with the international applica	ation.	
furr	ished by the applicant separa	ately from the interna	ational application,
			effect that it did not include ternational application as filed.
Tra	nscribed by this Authority		
4. With regard to the <b>title</b> , χ the	text is approved as submitted	d by the applicant	
the	text has been established by	this Authority to rea	d as follows:
5. With regard to the abstract,	text is approved as submitted	d by the applicant	
the Box	text has been established, ac	ccording to Rule 38.2 n one month from the	2(b), by this Authority as it appears in e date of mailing of this International
Sea	arch Report, submit comment	s to the Authority.	
6. The figure of the <b>drawings</b> to be pub	lished with the abstract is:		
	suggested by the applicant.		None of the figures.
bed	ause the applicant failed to s	uggest a figure.	
bed	eause this figure better charac	cterizes the invention	n.
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Box I	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This Inte	ernational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1.	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
2. X	Claims Nos.:  because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  See FURTHER INFORMATION SHEET PCT/ISA/210
3.	Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This Inte	ernational Searching Authority found multiple inventions in this international application, as follows:
1.	As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invitepayment of any additional fee.
3.	As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remari	The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.

International Application No. PCT/CA 98 \( D1010 \)

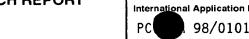
#### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

In view of the large number of compounds which are theoretically contained within the definition "proteasome inhibitor" of claims 1,10 and 14, the search had to be restricted on economic grounds to the general idea of the invention and to the compound explicitly mentioned in the description and in claims 6,11,15 (Art. 6 PCT; Guidelines Chapt.II.7 last sentence and Chapt.III,3.7).

Claims searched completely: 6,11,12,15-17

Claims searched incompletely:

1-5,7-10,13,14,18-20



c	INTERNATIONAL SEARCH		International App	lication No
			PC 98,	/01010
A. CLASSIF IPC 6	FICATION OF SUBJECT MATTER A61K31/40			
		ation and IDC		
	International Patent Classification (IPC) or to both national classification	ation and IPC	····	
	SEARCHED currentation searched (classification system followed by classification)	on symbols)	<del></del>	
IPC 6	A61K			
Documentat	ion searched other than minimum documentation to the extent that s	uch documents are incl	uded in the fields se	arched
Electronic da	ata base consulted during the international search (name of data ba	se and, where practical	, search terms used	
C. DOCUME	ENTS CONSIDERED TO BE RELEVANT	<u> </u>		
Category °	Citation of document, with indication, where appropriate, of the rel	evant passages		Relevant to claim No.
P,X	WANG X ET AL: "Role of proteason cell activation and proliferation JOURNAL OF IMMUNOLOGY, (1998 JAN (2) 788-801. JOURNAL CODE: IFB. 10022-1767., XP002093372 United States see the whole document	n." 15) 160		1-6
P,X	HIRSCH T ET AL: "Proteasome actioccurs at an early, premitochondr of thymocyte apoptosis." JOURNAL OF IMMUNOLOGY, (1998 JUL (1) 35-40. JOURNAL CODE: IFB. ISS 0022-1767., XP002093373 United States see the whole document	ial step 1) 161		10-17
▼ Furt	her documents are listed in the continuation of box C.	χ Patent family	members are listed	in annex.
"A" docume consider if ling of the consider if the consideration is the consideration of the consideration in the consideration is the consideration of the consideration in the consideration is the consideration of the consideration in the consideration is the consideration of the consideration in the consideration of the consideration is the consideration of the consideration of the consideration is the consideration of	ent which may throw doubts on priority claim(s) or is cited to establish the publication date of another n or other special reason (as specified) ent referring to an oral disclosure, use, exhibition or means ent published prior to the international filing date but an the priority date claimed	cited to understar invention  "X" document of partic cannot be considinvolve an inventi  "Y" document of partic cannot be consided document is combined to the consider of the consider of the cannot be considered.  "8" document member	d not in conflict with all the principle or the ular relevance; the dered novel or cannot we step when the do ular relevance; the dered to involve an indicate with one or moination being obvious of the same patent	the application but early underlying the claimed invention to econsidered to cument is taken alone claimed invention ventive step when the ore other such docuus to a person skilled
	actual completion of the international search		the international se	arch report
	5 February 1999	02/03/1	999	
i ivame and r	nailing address of the ISA	Authorized officer		

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Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016

Hoff, P



	with a second of the second of	-9.8/01010
C.(Continua	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Р,Х	X. WANG ET AL.: "RAPAMYCIN INHIBITS PROTEASOME ACTIVATOR EXPRESSION AND PROTEASOME ACTIVITY" EUR. J. IMMUNOL., vol. 27, no. 11, November 1997, pages 2781-2786, XP002093374 see the whole document	1-5, 7-10,13, 14,17-20
P , X	WO 98 13061 A (CV THERAPEUTICS INC ;JOLY ALISON (US); KERWAR SURESH (US); LUM ROB) 2 April 1998 see abstract see page 1, line 1 - line 15 see page 7, line 9 - line 19 see page 25, line 15 - page 26, line 9; claims; examples 2,5	1-5, 7-10,13, 14,17-20
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International Application No

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	Relevant to claim No.
MEYER S ET AL: "Cyclosporine A is an uncompetitive inhibitor of proteasome activity and prevents NF-kappaB activation." FEBS LETTERS, (1997 AUG 18) 413 (2) 354-8. JOURNAL CODE: EUH. ISSN: 0014-5793., XP002093375 Netherlands see the whole document	1-5, 7-10,13, 14,17-20
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CONNER E M ET AL: "Proteasome inhibition attenuates nitric oxide synthase expression, VCAM-1 transcription and the development of chronic colitis."  JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (1997 SEP) 282 (3) 1615-22.  JOURNAL CODE: JP3. ISSN: 0022-3565., XP002093378  United States see the whole document	10,13, 14,16,17
	MEYER S ET AL: "Cyclosporine A is an uncompetitive inhibitor of proteasome activity and prevents NF-kappaB activation." FEBS LETTERS, (1997 AUG 18) 413 (2) 354-8. JOURNAL CODE: EUH. ISSN: 0014-5793., XP002093375 Netherlands see the whole document

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ategory °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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A	IMAJOH-OHMI S ET AL: "Lactacystin, a specific inhibitor of the proteasome, induces apoptosis in human monoblast U937 cells." BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1995 DEC 26) 217 (3 1070-7. JOURNAL CODE: 9Y8. ISSN: 0006-291X., XP002093380 United States cited in the application	1-17

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